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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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10/618,338

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Jin-an Jiao

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FOLEY HOAG, LLP

PATENT GROUP, WORLD TRADE CENTER WEST

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EXAMINER

XIE, XIAOZHEN

ART UNIT

PAPER NUMBER

1646

MAIL DATE

DELIVERY MODE

09/06/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|------------------------------------|--|
| Office Action Summary | Application No. 10/618,338 | Applicant(s) JIAO ET AL. | |
| | Examiner Xiaozhen Xie | Art Unit 1646 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 June 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 37, 39-46, 54-60 and 65-67 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 37, 39-46, 54-60 and 65-67 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date <u>20070629</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

The Information Disclosure Statement (IDS) filed 29 June 2007 has been entered. Applicant's amendment of the claims received on 13 April 2007 has been entered.

Claims 1-36, 38, 47-53, 61-64 and 68 are cancelled. Claims 37, 39-46 and 54-60 and 65-67 are pending and under examination.

Specification

The objection to the specification for failing to update the cross-references in the first paragraph is withdrawn in response to applicant's amendment of the specification.

Claim Rejections Withdrawn

The rejection of claims 37, 42 and 54-61 under 35 U.S.C. 102(b) as being anticipated by Edgington et al. (US 5,223,427), is withdrawn in response to Applicant's amendment of the claims to recite that the antibody comprises a sequence represented by SEQ ID NO: 2 or 4.

The rejection of claims 37, 42 and 54-57 under 35 U.S.C. 102(b) as being anticipated by Fiore et al. (Blood, 1992, Vol. 80(12):3127-3134), is withdrawn in response to Applicant's amendment of the claims to recite that the antibody comprises a sequence represented by SEQ ID NO: 2 or 4.

The rejection of claims 43-46 and 65-67 under 35 U.S.C. 103(a) as being unpatentable over Fiore et al., or over US 5,223,427, in view of Queen et al. (US 5,693,762), is withdrawn in response to Applicant's amendment of the claims.

The objections to claims 43 and 48 for informalities are withdrawn in response to Applicant's amendment and cancellation of the claims.

Claim Rejections Maintained

The amended claims 37, 39-46 and 54-60 and 65-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for reducing TF levels to treat a solid tumor exhibiting TF expression, comprising administering to a mammal having the tumor cells a therapeutically effective amount of an antibody comprising the sequence of SEQ ID NO: 2 or SEQ ID NO: 4, or fragment thereof, does not reasonably provide enablement for treating any type of cancer that expresses TF (e.g., a non-tumor type of cancer such as a leukemia), nor provide enablement for administering to any mammal (including a mammal without a tumor). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicant argues that the claims, as amended, now require that the cancer exhibits TF expression, which obviate the rejection for lack of enablement.

Applicant's arguments have been fully considered but have not been found to be persuasive.

The amended claims are directed to a method for reducing TF levels to treat "a cancer exhibiting TF expression". The claims encompass treatment for any type of cancer that expresses TF, e.g., a solid tumor, and a non-tumor type of cancer such as leukemia. As set forth previously, the specification discloses the use of an anti-TF antibody for the treatment of a mammal having tumor cells that express TF, e.g. breast cancer, lung cancer, pancreatic cancer and ovarian cancer. The specification discloses detection of elevated TF expression on the surface of human lung carcinoma, human melanoma A375-C15 cells and human bladder carcinoma cells as compared to the non-cancerous tissue/cells. The art teaches that a direct correlation between elevated TF expression and advanced stages of malignancy has been reported in several different types of cancers, including non-small cell lung, breast, pancreatic ductal, colorectal, hepatocellular and prostate carcinoma, as well as melanoma (Yamashita et al. cited in the previous office action). Applicant, however, has not provided sufficient support for treating non-tumor type of cancer, such as leukemia, nor for treating any mammal, including one without tumor cells (i.e., prophylactic treatment). Ngo et al. (Int. J. Cancer, 2007, 120:1261-1267) teach that TF expressed on tumor cells can trigger intracellular signaling events through various pathways that can lead to tumor angiogenesis, proliferation and metastasis, and that the disruption of TF dependent signaling can

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effectively inhibit tumor cell migration, metastasis, and angiogenesis. Ngo et al. further demonstrated the anti-metastasis and anti-growth effects of an anti-TF antibody against human breast cancer in xenograft mouse models (see Abstract). The specification fails to provide sufficient guidance as to how to treat a non-tumor type of cancer, which is not mediated by the mechanisms of angiogenesis and metastasis. Without detailed guidance, the artisan would not be able to predict whether the claimed antibody is effective in treating a non-tumor type of cancer, or in prophylactic treatment.

Due to the large quantity of experimentation necessary to determine whether the anti-TF antibody recited in the claims is useful in treating or providing prophylactic treatment for any cancer exhibiting TF expression, including a non-tumor type cancer, the lack of direction/guidance presented in the specification, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes that the anti-cancer effects of anti-TF antibodies are mediated through inhibitions on tumor cell migration, metastasis, and angiogenesis, the breadth of the claims which encompasses all types of cancer exhibiting TF expression, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 37 recites "a sequence represented by SEQ ID NO: 2 or SEQ ID NO: 4". Since the specification provides no definition for the term "represented by", the metes and bounds of the claimed invention cannot be determined. Amending the claims to recite "the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 4" would obviate the rejection.

Claim 45 is indefinite for the recitation of "the humanized antibody". There is insufficient antecedent basis for this limitation in the claim.

Conclusion

NO CLAIM IS ALLOWED.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie, Ph.D whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph. D.
August 27, 2007


EILEEN B. O'HARA
PRIMARY EXAMINER